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CLINICAL USEFULNESS OF SERUM CA 125 IN PATIENTS WITH ENDOMETRIOSIS

(tumor marker/CA 125/endometriosis)

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Serum CA 125 levels in patients with endometriosis were elevated (35 U/ml or higher) in 88.9% (32/36). CA 125 levels correlated well with the response to Danazol treatment. Using this marker, myoma uteri and adenomyosis can be differentiated pre-operatively and the follow up with Danazol treatment in patients with endometriosis can be monitored.

An antigen specific to ovarian non-mucinous epithelial carcinoma, CA 125, has been used to diagnose ovarian cancer and its follow up after treatment. We measured serum CA 125 levels in patients with various gynecologic diseases to determine whether it is indeed specific to ovarian epithelial cancer. The usefulness of CA 125 as a tumor marker has been reported (1). Interestingly, considerably higher levels of CA 125 were observed in patients with endometriosis. We proposed that CA 125 can be used as an effective marker for differentiation of adenomyosis from myoma uteri (2). This report is a re-confirmation that CA 125 can serve as a pertinent marker for differentiation of adenomyosis from myoma uteri and follow up after Danazol treatment.

MATERIALS AND METHODS

Serum samples from 74 patients with uterine tumor (47 leiomyomata uteri, 19 adenomyosis, 4 adenomyosis with leiomyomata uteri and 4 adenomyosis with external endometriosis) and 16 with external endometriosis were obtained and kept at -20°C in the

Clinic of Obstetrics and Gynecology, Shimane Medical University Hospital. A histopathological diagnosis was made postoperatively in 83 women, and 7 patients with external endometriosis were diagnosed by manual examination and ultrasonic scanner. Huffmans and Beechams classifications were used as the clinical stage of endometriosis. CA 125 levels in serum were measured by the CA 125 Radioimmunoassay kit (Centocor, Inc., Malvern, PA, USA).

The least detectable levels of CA 125 was 8 U/ml. The mean CA 125 level (±S.D.) for healthy non-pregnant Japanese women and the cut-off value were 14.7±9.3 U/ml and 34 U/ml, respectively (3). These values were used as control. Student's t-test was used for statistical analysis ($P<0.05$).

RESULTS

Distribution of CA 125 in serum of healthy non-pregnant women, patients with myoma uteri and with endometriosis pre-operatively is shown in Fig.1. Two (4.3%) of 47 patients with leiomyomata uteri had CA 125 levels in excess of 34 U/ml. The mean CA 125 levels (±S.D.) for 47 patients with leiomyomata uteri were 20.6±9.9 U/ml. Statistically, no difference in the mean CA 125 level was observed between control and patients with leiomyomata uteri. On the other hand, thirty-two (88.9%) of 36 patients with endometriosis, especially 26 (96.3%) of 27 patients with adenomyosis, had CA 125 levels in excess of 34 U/ml. Positive ratio (>34 U/ml) of serum CA 125 levels for patients with endometriosis was higher than that for healthy women and patients with leiomyomata uteri. The mean CA 125 levels (±S.D.) in 19 patients with adenomyosis alone, for 4 patients with adenomyosis and leiomyomata uteri, for 4 patients with adenomyosis and external endometriosis and for 9 patients with external endometriosis alone were 90.3±53.7, 75.8±38.3, 316.3±239.3 and 48.9±20.3 U/ml, respectively. The mean CA 125 level in patients with adenomyosis and external endometriosis was the highest value of 36 patients with endometriosis. On the contrary, the mean CA 125 level in patients with external endometriosis alone was the lowest value of 36 patients with endometriosis.

Changes in serum CA 125 levels in 15 patients with adenomyosis are shown in Fig.2. Positive serum CA 125 levels (>34 U/ml) pre-operatively were reduced postoperatively and were

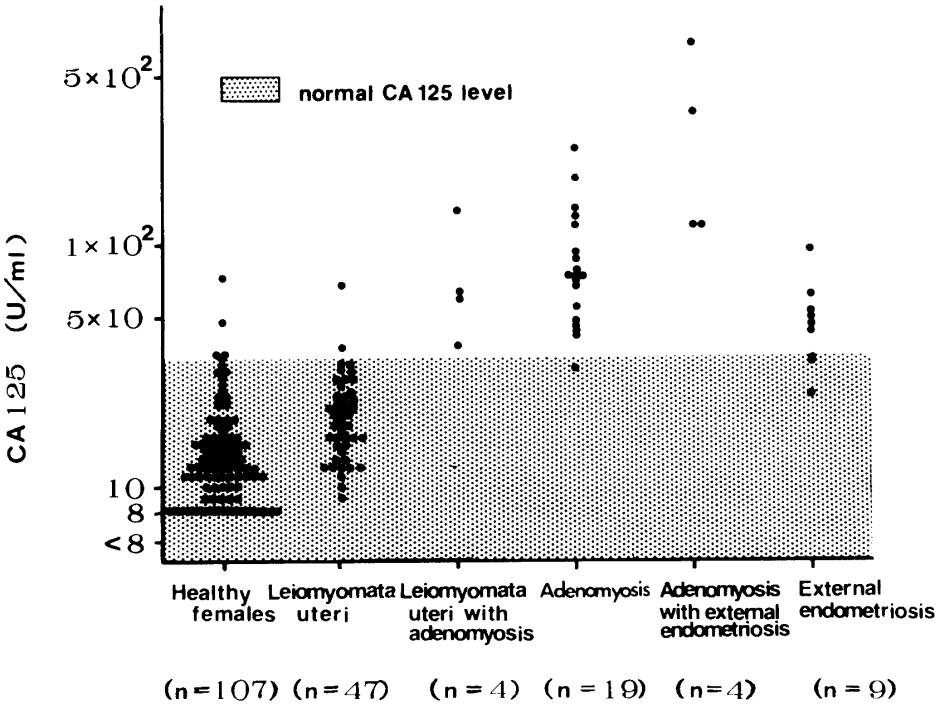

Fig.1. Serum levels of CA 125

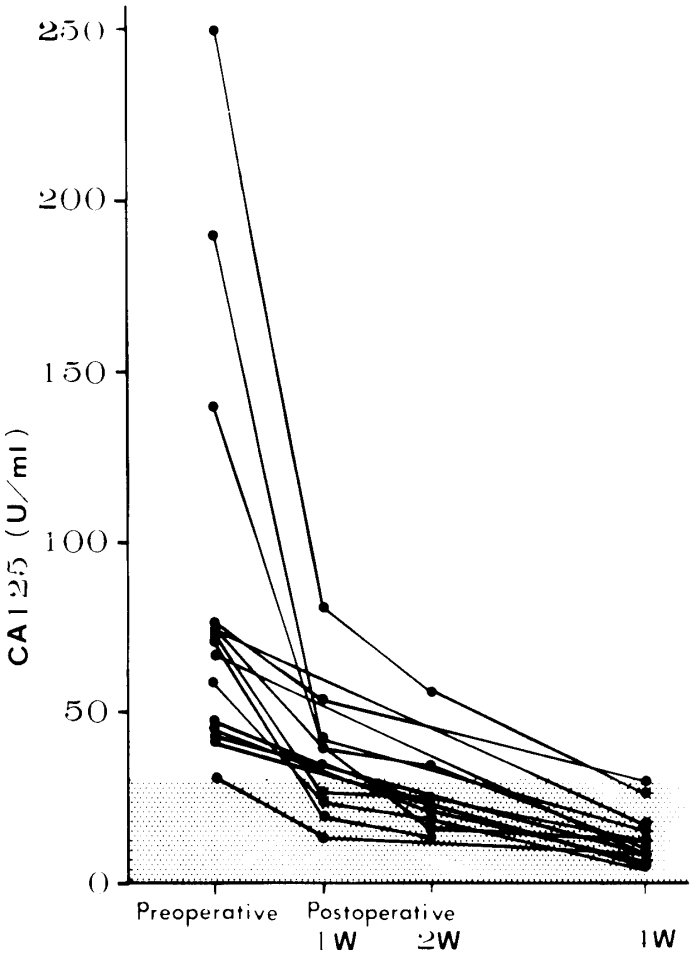

Fig.2. Changes of CA 125 levels in sera of patients with adenomyosis

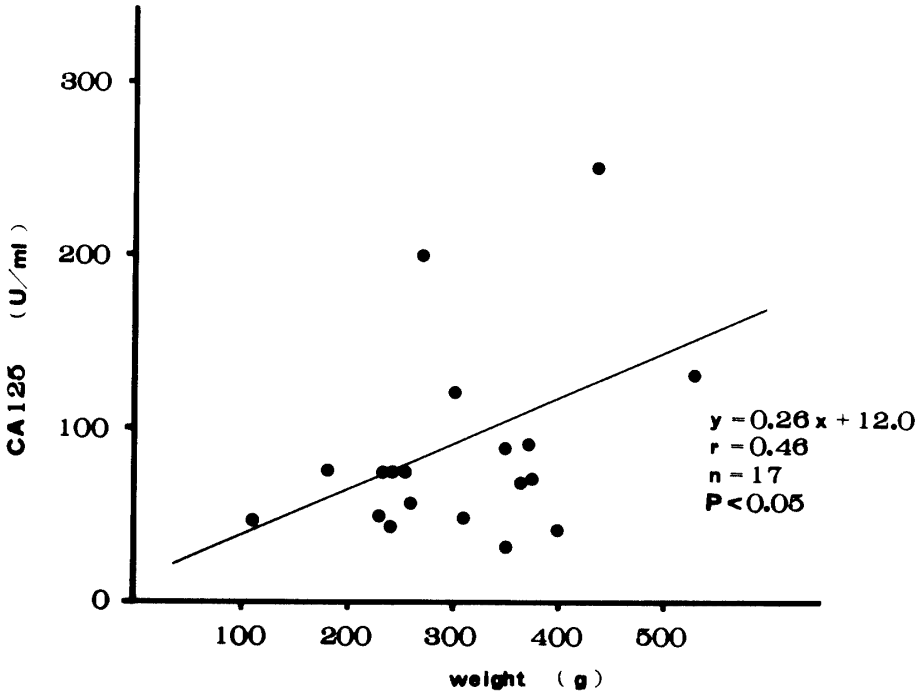

Fig.3. Correlation between serum CA 125 levels and the weight of uterus in patients with adenomyosis

reduced from about one half to about one ninth at one week after hysterectomy. The levels were below 34 U/ml within 4 weeks after operation in all patients.

The correlation between serum CA 125 levels at pre-operation and the weight of uterus at postoperation in patients with adenomyosis is shown in Fig.3. Statistically, the regression line ($y=0.26x+12.0$) was determined ($P<0.05$). The heavier the uterus was, the higher the serum CA 125 levels were.

Changes in serum CA 125 levels in 6 patients with external endometriosis pre- and postoperatively are shown in Fig.4. For all patients, 400 mg/day of Danazol was administered since one week after the surgery. In one, there was a transient increase in CA 125 level postoperatively. High serum CA 125 levels were reduced to below 34 U/ml within 4 weeks after the surgery, in all patients. These women are on Danazol treatment and to date, the serum CA 125 levels are not over 34 U/ml.

The relation between serum CA 125 levels and the clinical stage of endometriosis is shown in Fig.5. A significant difference in serum CA 125 levels between Huffman III stage,

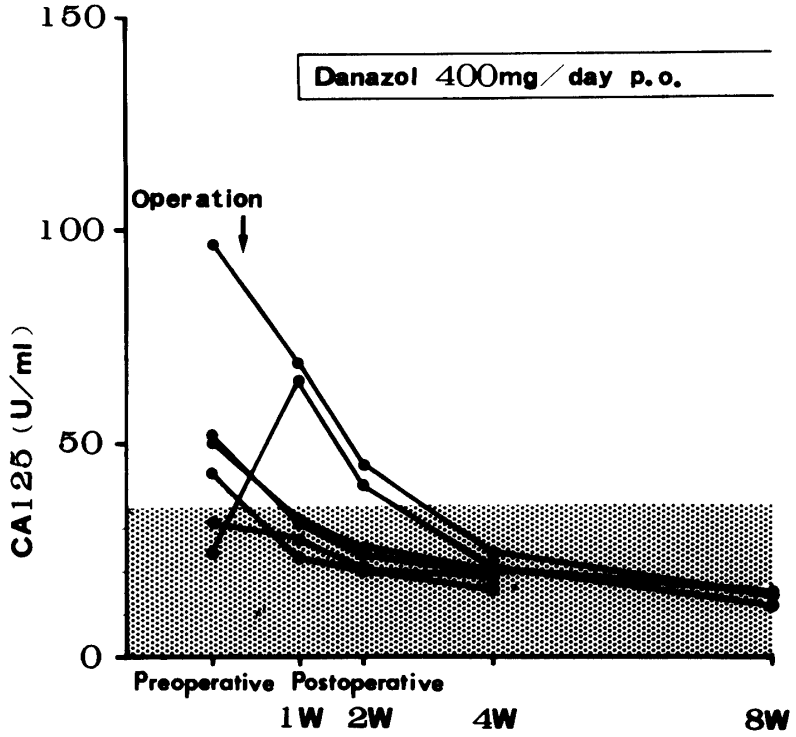

Fig.4. Changes of CA 125 levels in sera of patients with external endometriosis

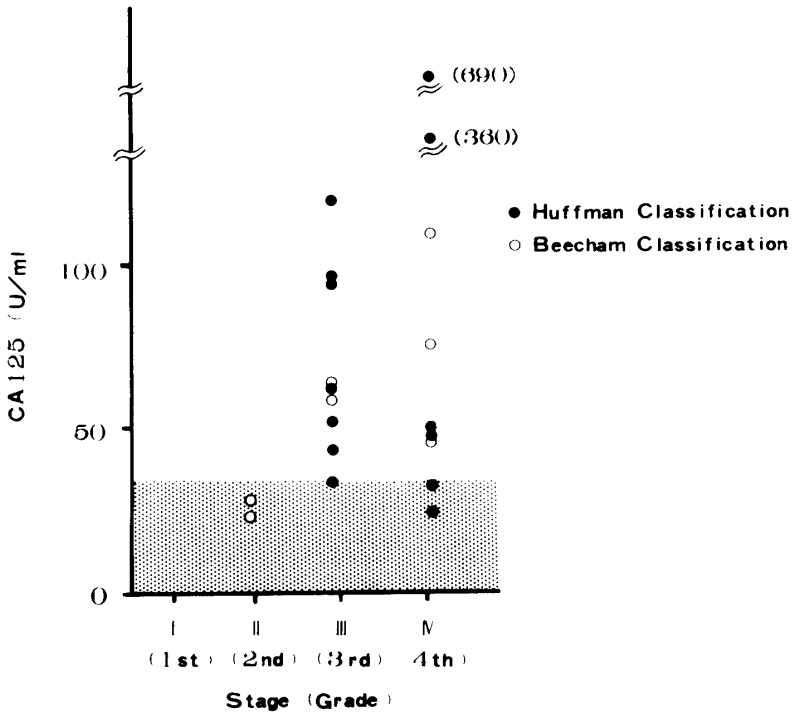

Fig.5. Serum CA 125 levels and the stage of endometriosis

including Beecham 3 grade and Huffman IV stage, including Beecham 4 grade was not observed. But, serum CA 125 levels in patients with Beecham 3 and 4 grade of endometriosis were higher than that in patients with Beecham 2 grade of endometriosis.

DISCUSSION

CA 125 was detected on surface epithelial cells of ovarian epithelial tumors (4). CA 125 is a promising clinical marker of diagnosing and monitoring the response to treatment in patients with nonmucinous epithelial ovarian carcinoma (1,5,6). CA 125 levels in case of tumor with other histology (i.e. endometrioid adenocarcinoma of ovary and adenocarcinoma of the uterine endometrium) were frequently over 34 U/ml (4,7). As CA 125 may be related histologically to endometrium of the uterus, we attempted to differentiate myoma uteri from adenomyosis, by assessing CA 125, pre-operatively (2). We have now reconfirmed that myoma and adenomyosis could be differentiated pre-operatively by determining serum levels of CA 125. Danazol proved to be an effective agent in conservative treatment for patients with endometriosis, however, the serological marker of the response to Danazol treatment in patients with endometriosis has heretofore not been determined. We propose that use of CA 125 as a marker to monitor the response to Danazol treatment in patients with endometriosis should produce pertinent results.

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